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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,799	03/04/2004	Sacha Adrianus Fokke Taco Van Hijum	2001-1043-2	3865
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YOUNG & THOMPSON 745 SOUTH 23RD STREET 2ND FLOOR ARLINGTON, VA 22202			EXAMINER PROUTY, REBECCA E	
			ART UNIT 1652	PAPER NUMBER

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No. 10/791,799	Applicant(s) VAN HIJUM ET AL.	
	Examiner Rebecca E. Prouty	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 2 and 7-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/604,958.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>3/04</u> . | 6) <input type="checkbox"/> Other: _____ |

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Applicant's election with traverse of Group II, Claims 1 and 3-6 in the reply filed on 11/13/06 is acknowledged. The traversal is on the ground(s) that the subject matter of Groups I-IV are sufficiently closely related that a search and examination of the entire application can be made without a serious burden and that Groups I and II are not patentably distinct as the methods do not comprise different steps, utilize different products, and produce different results.. This is not found persuasive because while the search for the non-elected groups would overlap that of the elected group it would not be coextensive. Furthermore, Groups I and II comprise different steps, utilize different products, and produce different results. As previously stated. Note, patentable distinctness of the methods would have required a showing of only one of these and not all three, but in the instant case all three of these differ between the two methods. Group I utilizes bacteria comprising a inulosucrase enzyme to produce inulin (a fructan having β (2-1) linked fructose residues) while Group II utilizes a bacteria comprising a levansucrase enzyme to produce levan (a fructan having β (2-6) linked fructose residues). Note levan and inulin have different chemical structures and different properties and uses. Furthermore, while there are bacteria which comprise both a inulosucrase and a levansucrase, there are

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many bacteria which produce only one of these. Thus the group of products used differs between the two Groups and the search required for each is different as art which applies to one of these groups may not be relevant to the other.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2 and 7-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/13/06.

Claims 1 and 4-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of using a genus of *Lactobacillus* strains capable of producing a fructosyltransferase for the production of levan. The specification teaches the structure of only a single representative species of such *Lactobacillus* strains (i.e.,

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Lactobacillus reuteri strain 121). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of producing a fructosyltransferase capable of producing levan. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1 and 3-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing levan using *Lactobacillus reuteri* strain 121 or a microorganism transformed with a nucleic acid encoding the levansucrase of SEQ ID NO:11, does not reasonably provide enablement for methods of producing levan using any *Lactobacillus* strain capable of producing a fructosyltransferase producing a fructan having β (2-6) linked fructose residues or a fructosyltransferase having 85% identity to SEQ ID NO:11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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Claims 1 and 3-6 are so broad as to encompass methods of using any *Lactobacillus* strain capable of producing any fructosyltransferase producing a fructan having β (2-6) linked fructose residues or any fructosyltransferase having 85% identity to SEQ ID NO:11. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of *Lactobacillus* strain and fructosyltransferase enzymes broadly encompassed by the methods of the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to only one specific fructosyltransferase capable of producing a fructan having β (2-6) linked fructose residues. Furthermore, while there are many *Lactobacillus* strains known, *Lactobacillus reuteri* strain 121 is the only known strain which appears to produce a levansucrase. See for example page 3012 of Van Geel-Schutten et al. (1999)

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which states that "Levan synthesis in lactic acid bacteria has been reported only for *Streptococcus* species.. The present study is the first report of the synthesis of a levan type of polysaccharide in the genus *Lactobacillus*". As such the presence of a levansucrase enzyme is a rarity within the genus and the specification provides no guidance for selecting other strains encoding a suitable enzyme.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass methods of use of enormous numbers of *Lactobacillus* strains and fructosyltransferase enzymes because the specification does not establish: (A) regions of the protein structure which may be modified without effecting

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fructosyltransferase activity; (B) the general tolerance of fructosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any fructosyltransferase residues with an expectation of obtaining the desired biological function; (D) suitable strains of *Lactobacillus* which produce a levansucrase or means of identifying suitable strains; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of use of enormous numbers of *Lactobacillus* strains and fructosyltransferase enzymes. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of *Lactobacillus* strains and fructosyltransferase enzymes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by either of Van Geel-Schutten et al. (1998) or Van Geel-Schutten et al. (1999).

Each of van Geel-Schutten et al. (1999) and van Geel-Schutten et al. (1998) teach the cultivation of *Lactobacillus reuteri* strain LB 121, and use this strain for the synthesis of levan from either sucrose or raffinose using both washed cells and culture supernatant (see particularly Table 3 of van Geel-Schutten et al. (1999) and Table 2 of van Geel-Schutten et al. (1998). As the strain cited in each of these references is identical to that used by applicants, the methods of van Geel-Schutten et al. (1999) and van Geel-Schutten et al. (1998) inherently use the enzymes of SEQ ID NO: 11 and anticipate Claim 3. Furthermore, each of van Geel-Schutten et al. (1999) and van Geel-Schutten et al. (1998) teach the further hydrolysis of the fructan produced and van Geel-Schutten et al. (1999) also teach the methylation of the fructan further anticipating Claim 6.

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of van Geel-Schutten et al. (1999) and van Geel-Schutten et al. (1998).

van Geel-Schutten et al. (1999) and van Geel-Schutten et al. (1998) are discussed above. Each of these references further teach that extracellular polysaccharides such as those produced by the *Lactobacillus reuteri* strain LB 121 find use as food thickeners and that lactic acid bacteria themselves often also contribute positively to the taste, smell or preservation of food products.

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Therefore, it would have been obvious to one of ordinary skill in the art to combine the extracellular polysaccharides produced by either of van Geel-Schutten et al. (1999) and van Geel-Schutten et al. (1998) and optionally other lactic acid bacteria such as other *Lactobacillus* strains with additional components of such foods.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 3-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over

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claims 7 and 8 of U.S. Patent No. 6,730,502. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1, 3 and 6 herein and claims 7 and 8 of U.S. Patent No. 6,730,502 are all directed to methods of making levan comprising reacting sucrose with a microorganism producing a levansucrase enzyme of SEQ ID NO:11 or variants thereof and further chemically modifying the levan produced. The claims differ in that claims 1, 3 and 6 herein recite that the microorganism used is specifically a *Lactobacillus* strain whereas claims 7 and 8 of U.S. Patent No. 6,730,502 recite that the microorganism used is any microorganism transformed with a nucleic acid encoding the levansucrase of SEQ ID NO:11 or variants thereof. However, as the fructans produced by the process of claims 7 and 8 of U.S. Patent No. 6,730,502 have use within food products and *Lactobacillus* are well known to be microorganisms with GRAS status in the food industry, it would have been obvious to one of skill in the art to use a *Lactobacillus* strain as the recombinant production host in order ensure that the fructan product could be safely introduced into food products. Furthermore, as extracellular polysaccharides such as levan are well known to have use as food thickeners and lactic acid bacteria themselves are known to contribute positively to the taste, smell or preservation of food products,

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it would have been obvious to one of ordinary skill in the art to combine the extracellular polysaccharides produced by the process of claims 7 and 8 of U.S. Patent No. 6,730,502 and optionally other lactic acid bacteria such as other *Lactobacillus* strains with additional components of such foods. As such claims 4 and 5 herein would have also been obvious over claims 7 and 8 of U.S. Patent No. 6,730,502.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Rebecca Prouty
Primary Examiner
Art Unit 1652